09/418,221

for reducing cerebral infarct vol.

L4 ANSWER 3 OF 3 CA COPYRIGHT 2000 ACS
ACCESSION NUMBER: 129:90287 CA
TITLE: Sonic hedgehog protein: a novel approach to the treatment of neurodegenerative disorders?
AUTHOR(S): Pang, Kevin; Ingolia, Thomas D.
CORPORATE SOURCE: Ontogeny Inc., Cambridge, MA, USA
SOURCE: CNS Drugs (1998), 9(4), 253-259
CODEN: CNDREF; ISSN: 1172-7047
PUBLISHER: Adis International Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sonic hedgehog is a member of a newly discovered family of mols. that are active during development in vertebrates. Sonic hedgehog induces development of key CNS neuronal cell types, including the dopaminergic neurons that are destroyed in Parkinson's disease. In addn. to developmental-inducing activity, Sonic hedgehog has neurotrophic and neuroprotective activities on many of these same cell types. These activities suggest interesting clin. potentials for Sonic hedgehog in neurodegenerative diseases such as Parkinson's disease and in acute CNS trauma such as stroke.

=> d his

(FILE 'HOME' ENTERED AT 15:59:51 ON 18 NOV 2000)

FILE 'CA' ENTERED AT 15:59:55 ON 18 NOV 2000
L1 0 S PTC(10W)THERPEUTIC#
L2 309 S PTC(10W)THER?
L3 1 S L2 AND STROKE
L4 3 S NEUROPROTEC?(10W)HEDGEHOG(10W)PROTEIN#

=> s l2 not l3

L5 308 L2 NOT L3

=> s l5 and ptc

2309 PTC
L6 308 L5 AND PTC

=> s l6 and patched binding peptide

536 PATCHED
612303 BINDING
236178 PEPTIDE
0 PATCHED BINDING PEPTIDE
(PATCHED(W)BINDING(W)PEPTIDE)
L7 0 L6 AND PATCHED BINDING PEPTIDE

=> s l6 and neuron?

133007 NEURON?
L8 2 L6 AND NEURON?

=> d l8 1-2 ibib ab

L8 ANSWER 1 OF 2 CA COPYRIGHT 2000 ACS
ACCESSION NUMBER: 133:41366 CA
TITLE: The normal patched allele is expressed in medulloblastomas from mice with heterozygous germ-line mutation of patched
AUTHOR(S): Wetmore, Cynthia; Eberhart, Derek E.; Curran, Tom
CORPORATE SOURCE: Departments of Developmental Neurobiology and Hematology/Oncology, St. Jude Children's Research Hospital, Memphis, TN, 38105, USA
SOURCE: Cancer Res. (2000), 60(8), 2239-2246
CODEN: CNREA8; ISSN: 0008-5472
PUBLISHER: American Association for Cancer Research
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Defects in a developmental signaling pathway involving mammalian homologs of the Drosophila segment polarity gene, patched (**ptc**) and its ligand, sonic hedgehog (shh), contribute to tumor formation in several tissues. Recently, a subset of medulloblastoma, the most common malignant brain tumor in children, was found to contain somatic mutations in the human **ptc** gene. In addn., basal cell nevus syndrome (BCNS), or Gorlin syndrome, which is characterized by developmental anomalies and a predisposition to skin and nervous system malignancies, is assocd. with germ-line mutation of **ptc**. Targeted disruption of both alleles of **ptc** in mice results in embryonic lethality. However, **ptc**+/- mice survive and develop spontaneous cerebellar brain tumors, suggesting that **ptc** may function as a tumor suppressor gene. Therefore, we investigated **ptc**+/- mice as a model for human medulloblastoma. We report that 14% of **ptc**+/- mice develop central nervous system tumors in the posterior fossa by 10 mo of age, with peak tumor incidence occurring between 16 and 24 wk of age. The tumors exhibited several characteristics of human medulloblastoma, including expression of intermediate filament proteins specific for **neurons** and glia. Full-length **ptc** mRNA was present in all tumors analyzed, indicating that **there** was no loss of heterozygosity at the **ptc** locus. Nucleotide sequence of **ptc** mRNA from four tumors failed to identify any mutations. However, a comparison of the normal **ptc** sequence from C57BL/6 and 129Sv mice did reveal several polymorphisms. High levels of gli1 mRNA and protein were detected in the tumors, suggesting that the shh/**ptc** pathway was activated despite the persistence of **ptc** expression. These data indicate that haploinsufficiency of **ptc** is sufficient to promote oncogenesis in the central nervous system.

REFERENCE COUNT: 49
REFERENCE(S):
(1) Aszterbaum, M; J Investig Dermatol 1998, V110, P885 CA
(3) Capdevila, J; EMBO J 1994, V13, P71 CA
(4) Chen, Y; Cell 1996, V87, P553 CA
(7) Dahmane, N; Development (Camb) 1999, V126, P3089 CA
(8) Dahmane, N; Nature (Lond) 1997, V389, P876 CA
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 2 CA COPYRIGHT 2000 ACS
ACCESSION NUMBER: 130:205165 CA
TITLE: Regulation of muscle tissue formation and/or maintenance with hedgehog proteins and **ptc** **therapeutics** and treatment or prevention of muscular disorders
INVENTOR(S): Bladgen, Chris S.; Currie, Peter D.; Ingham, Philip

W.; Hughes, Simon M.
PATENT ASSIGNEE(S): Ontogeny, Inc., USA
SOURCE: PCT Int. Appl., 130 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9910004	A2	19990304	WO 1998-US17922	19980828
WO 9910004	A3	19990527		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9891252	A1	19990316	AU 1998-91252	19980828
EP 1009424	A2	20000621	EP 1998-943462	19980828
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-57394 19970829
WO 1998-US17922 19980828

OTHER SOURCE(S): MARPAT 130:205165

AB The present application relates to a method for modulating the formation and/or maintenance of muscle tissue by ectopically contacting muscle cells, esp. muscle stem/progenitor cells, in vitro or in vivo, with a hedgehog therapeutic or **ptc therapeutic** in an amt. effective to alter the growth state of the treated cells. The hedgehog therapeutic comprises a hedgehog protein modified with one or more lipophilic moieties, e.g., sterols, fatty acids, or arom. hydrocarbons. The **ptc therapeutics** mimic hedgehog-mediated patched signal transduction by binding to patched or altering localization, protein-protein binding and/or enzymic activity of intracellular proteins involved in patched signal transduction. Such therapeutics included antisense oligonucleotides and protein kinase A inhibitors. Expts. in zebrafish suggested that SHH may initiate slow myoblast formation but that continued exposure is not required to trigger terminal differentiation of slow muscle fibers.

=> d his

(FILE 'HOME' ENTERED AT 15:59:51 ON 18 NOV 2000)

FILE 'CA' ENTERED AT 15:59:55 ON 18 NOV 2000
L1 0 S PTC(10W)THERPEUTIC#
L2 309 S PTC(10W)THER?
L3 1 S L2 AND STROKE
L4 3 S NEUROPROTEC?(10W)HEDGEHOG(10W)PROTEIN#
L5 308 S L2 NOT L3
L6 308 S L5 AND PTC
L7 0 S L6 AND PATCHED BINDING PEPTIDE
L8 2 S L6 AND NEURON?

=> log y

COST IN U.S. DOLLARS SINCE FILE ENTRY TOTAL SESSION

FULL ESTIMATED COST	31.87	32.02
DISCOUNT AMOUNTS ([redacted] QUALIFYING ACCOUNTS)	SIN[redacted] FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-2.65	-2.65

STN INTERNATIONAL LOGOFF AT 16:05:52 ON 18 NOV 2000